

This Page Is Inserted by IFW Operations  
and is not a part of the Official Record

## **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning documents *will not* correct images,  
please do not report the images to the  
Image Problem Mailbox.**



Figure 1: Sedation Model

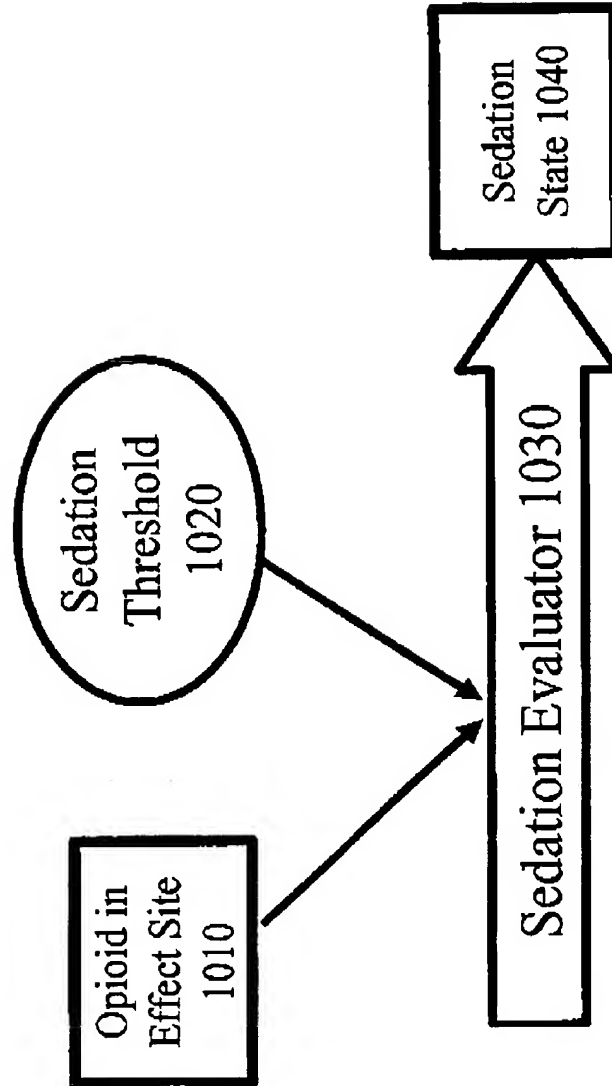


Figure 2: Ventilatory Depression Model

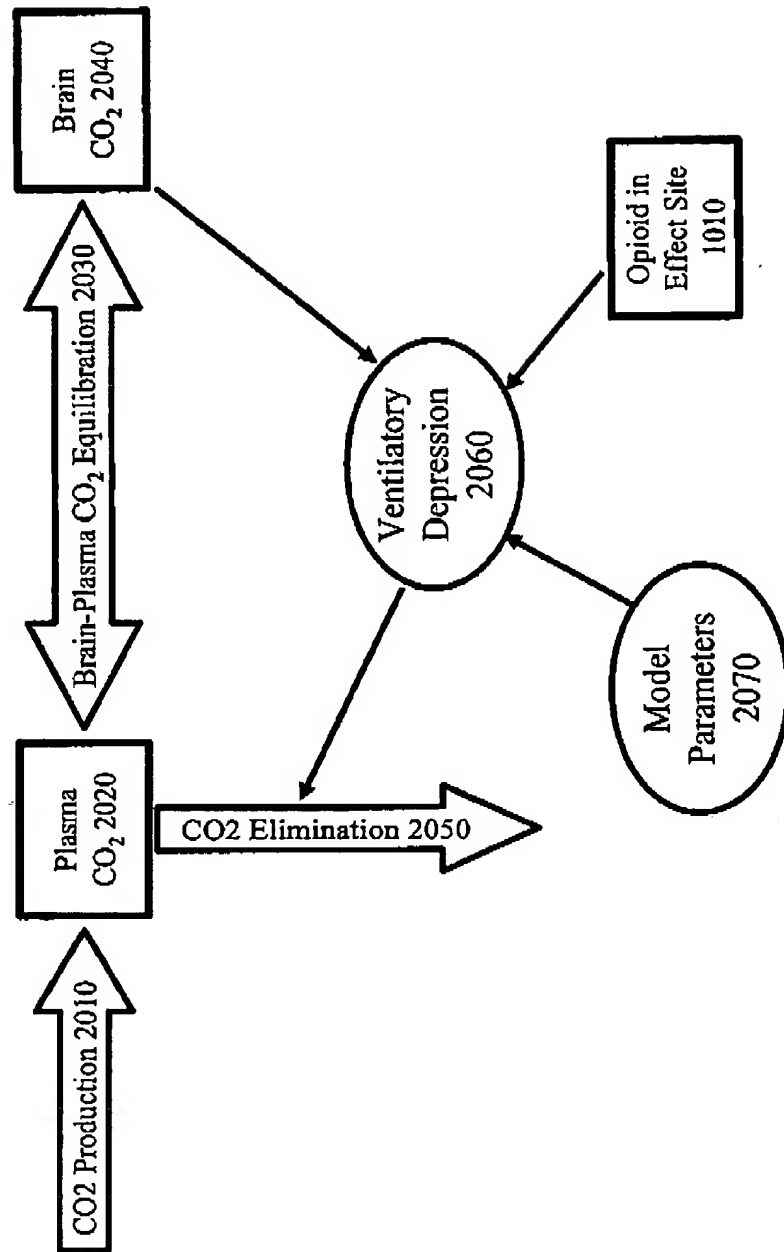


Figure 3: Device Model

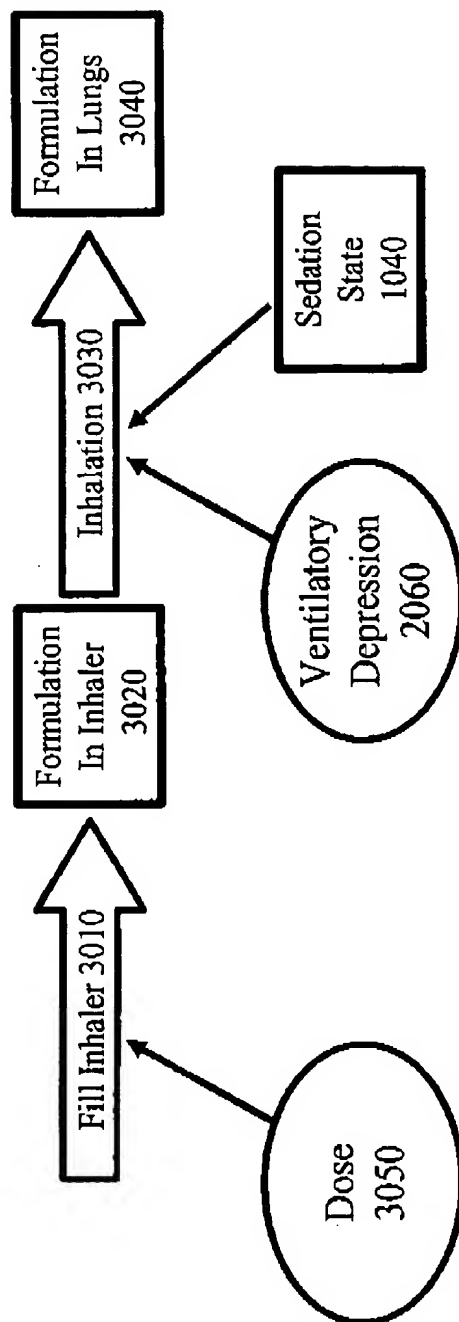
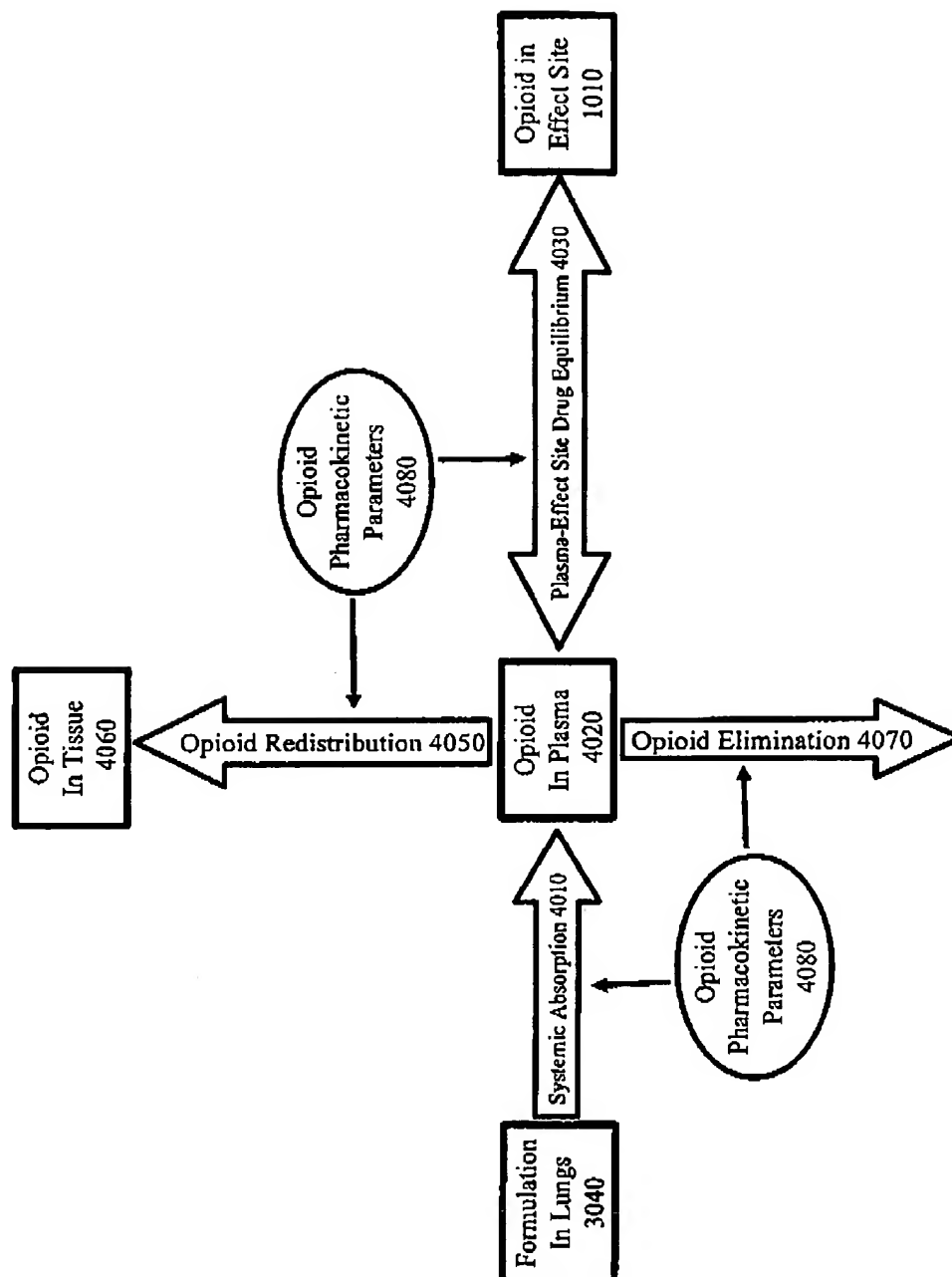
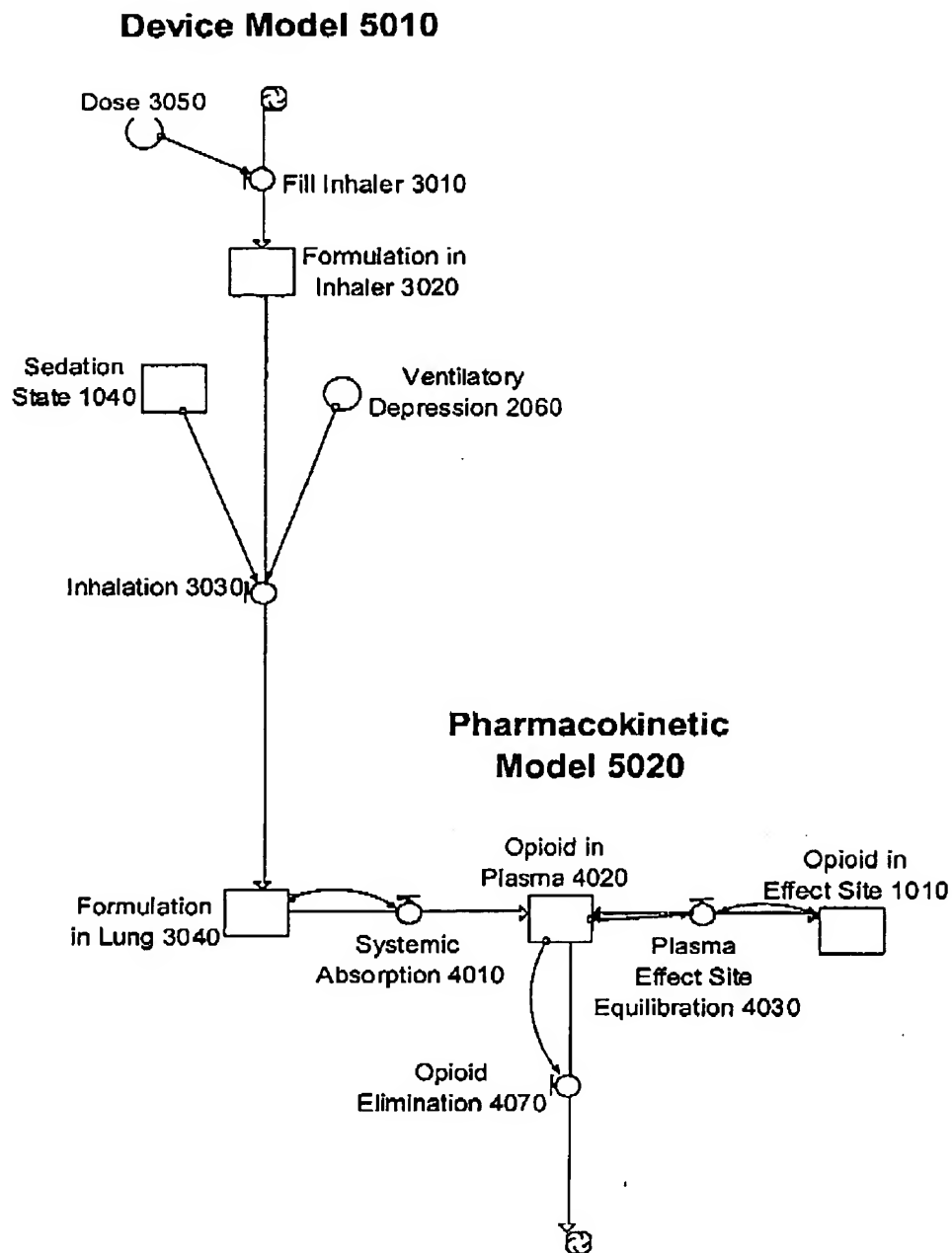
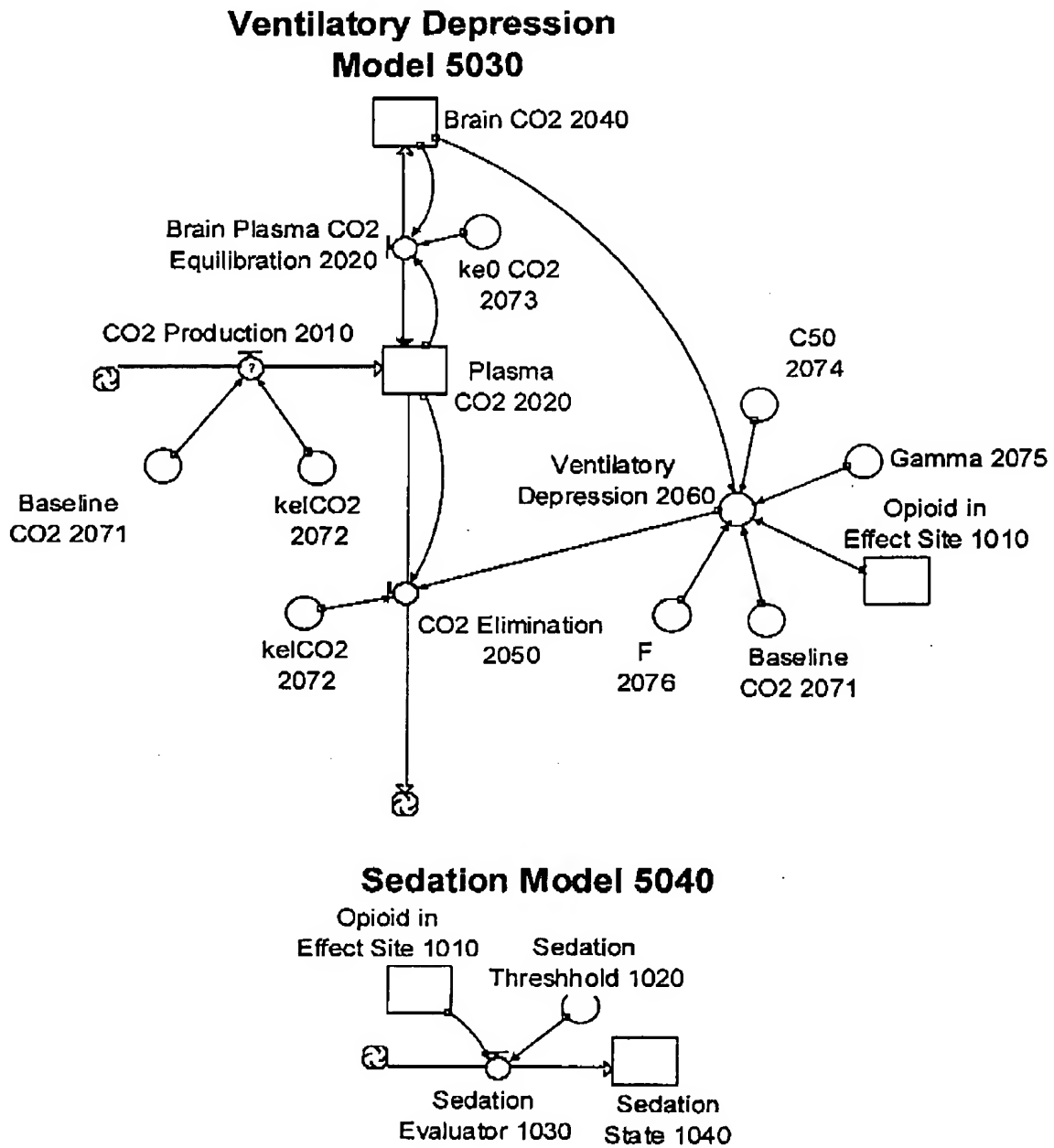


Figure 4: Pharmacokinetic Model



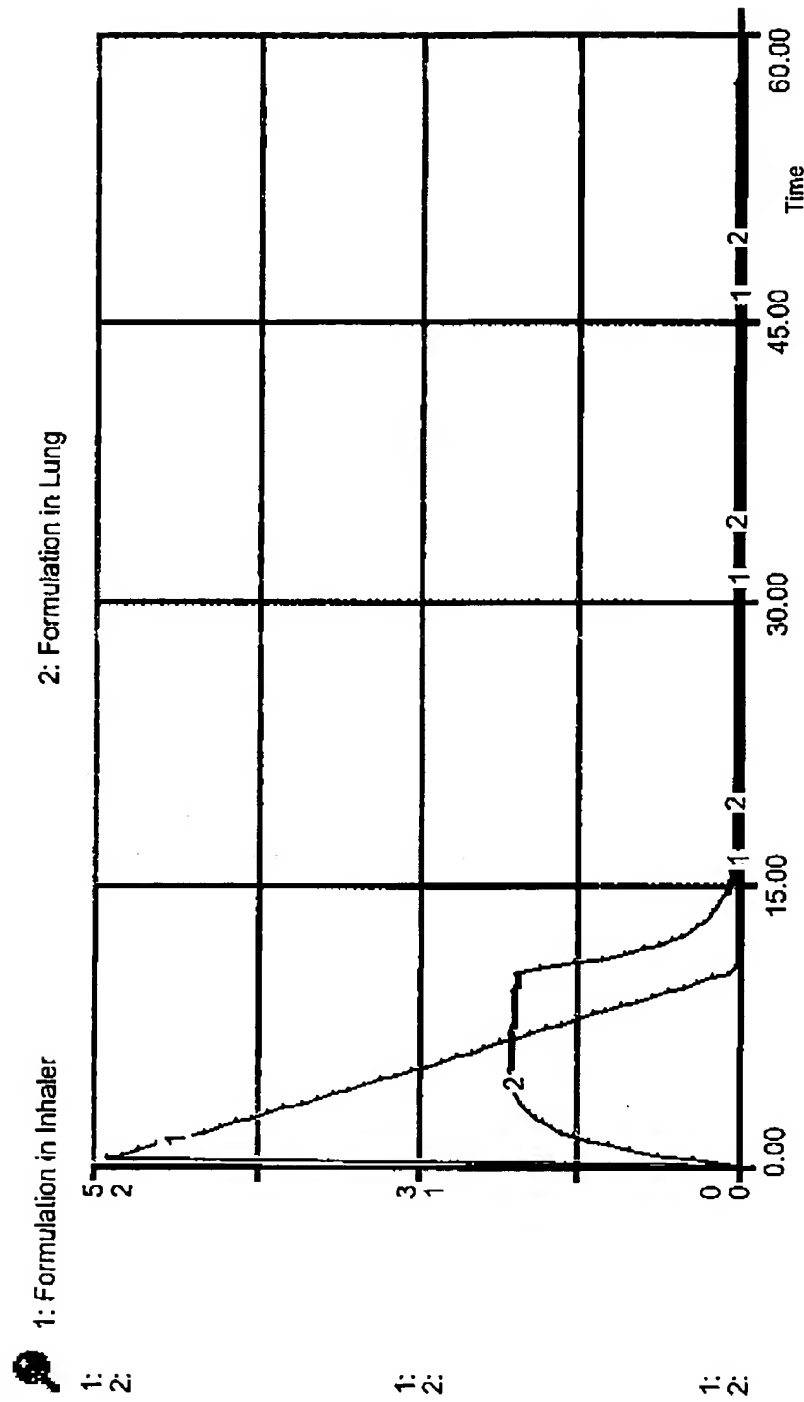
**Figure 5A**

5/27

**Figure 5B**

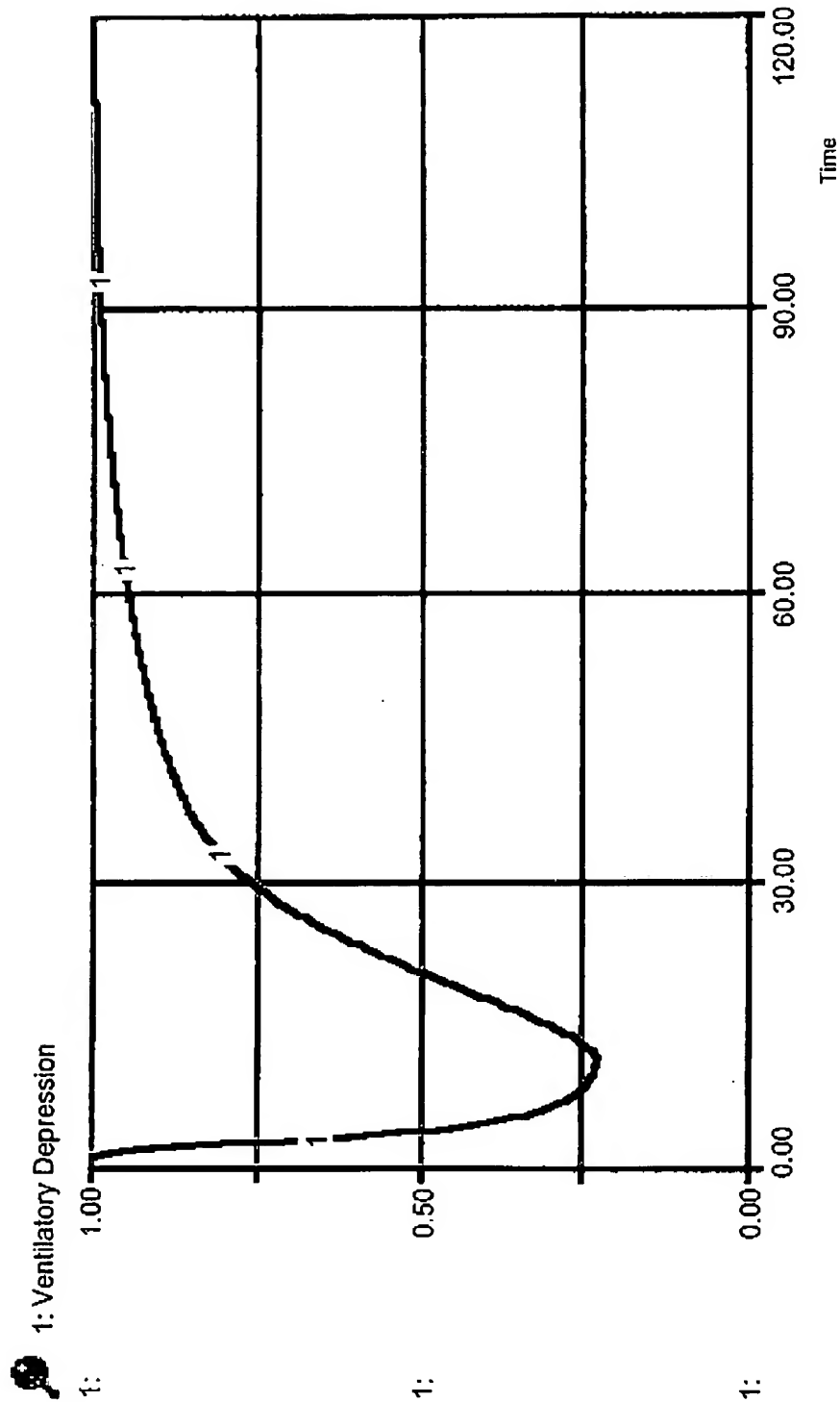
6/27

Figure 6



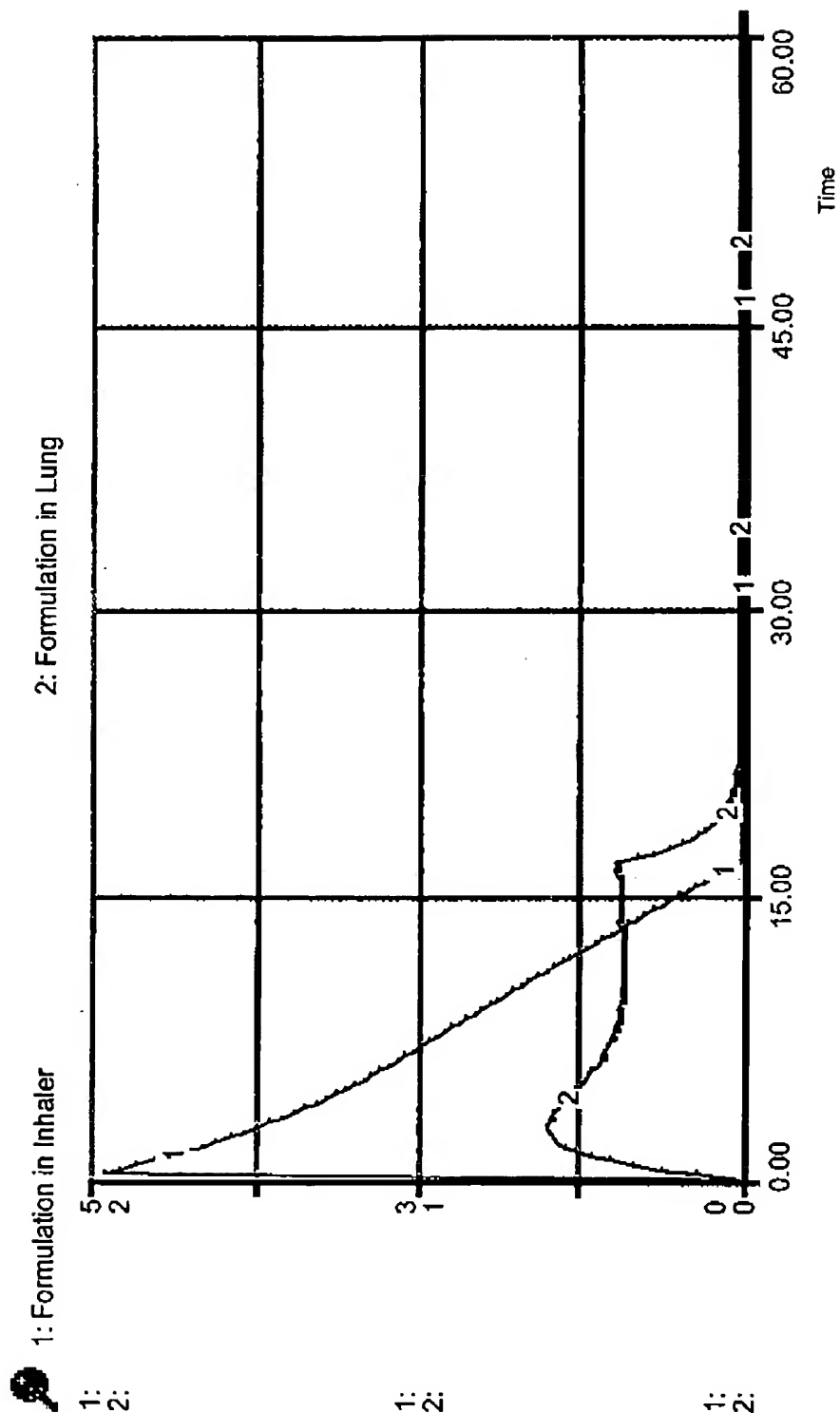
7/27

Figure 7



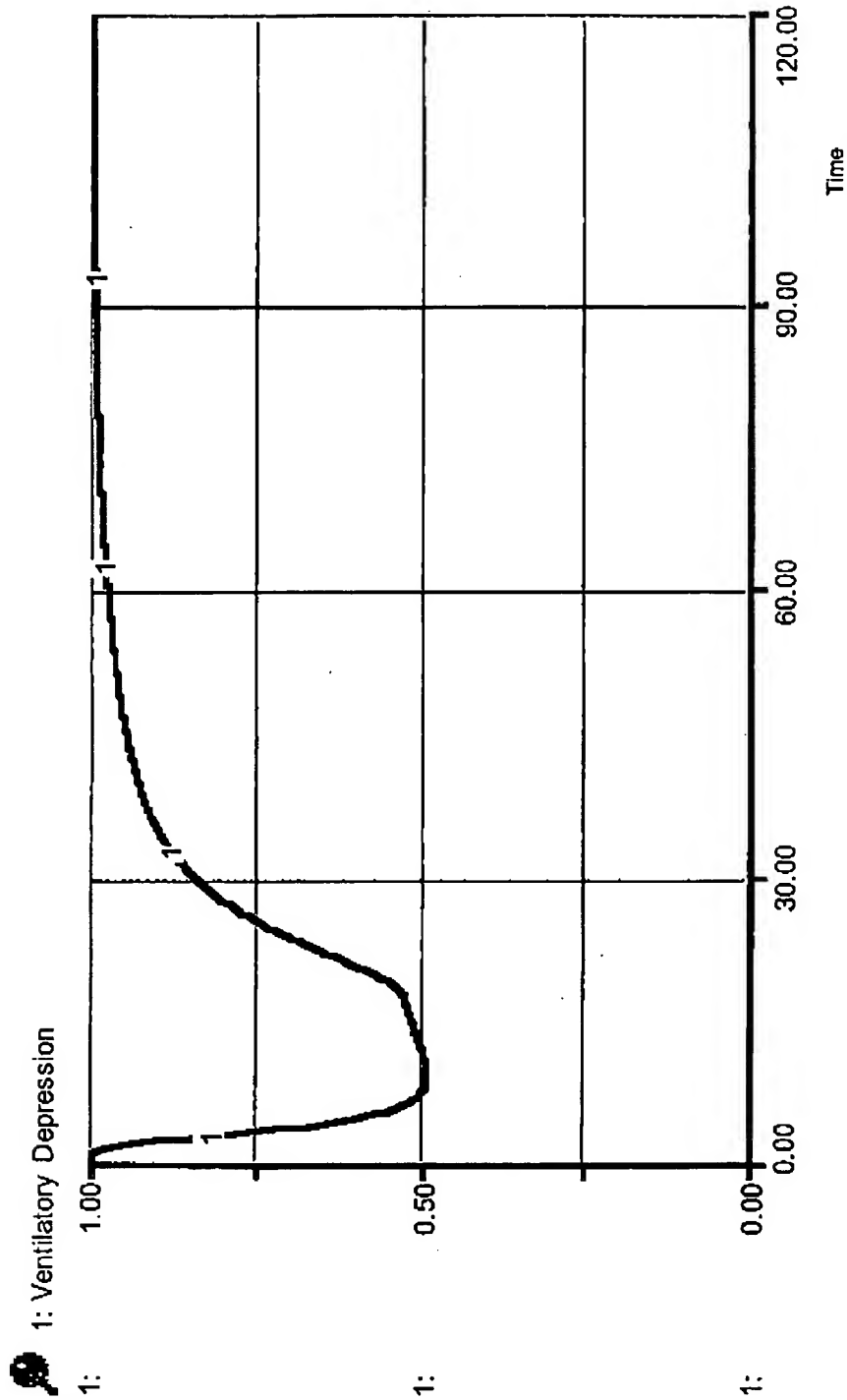
8/27

Figure 8



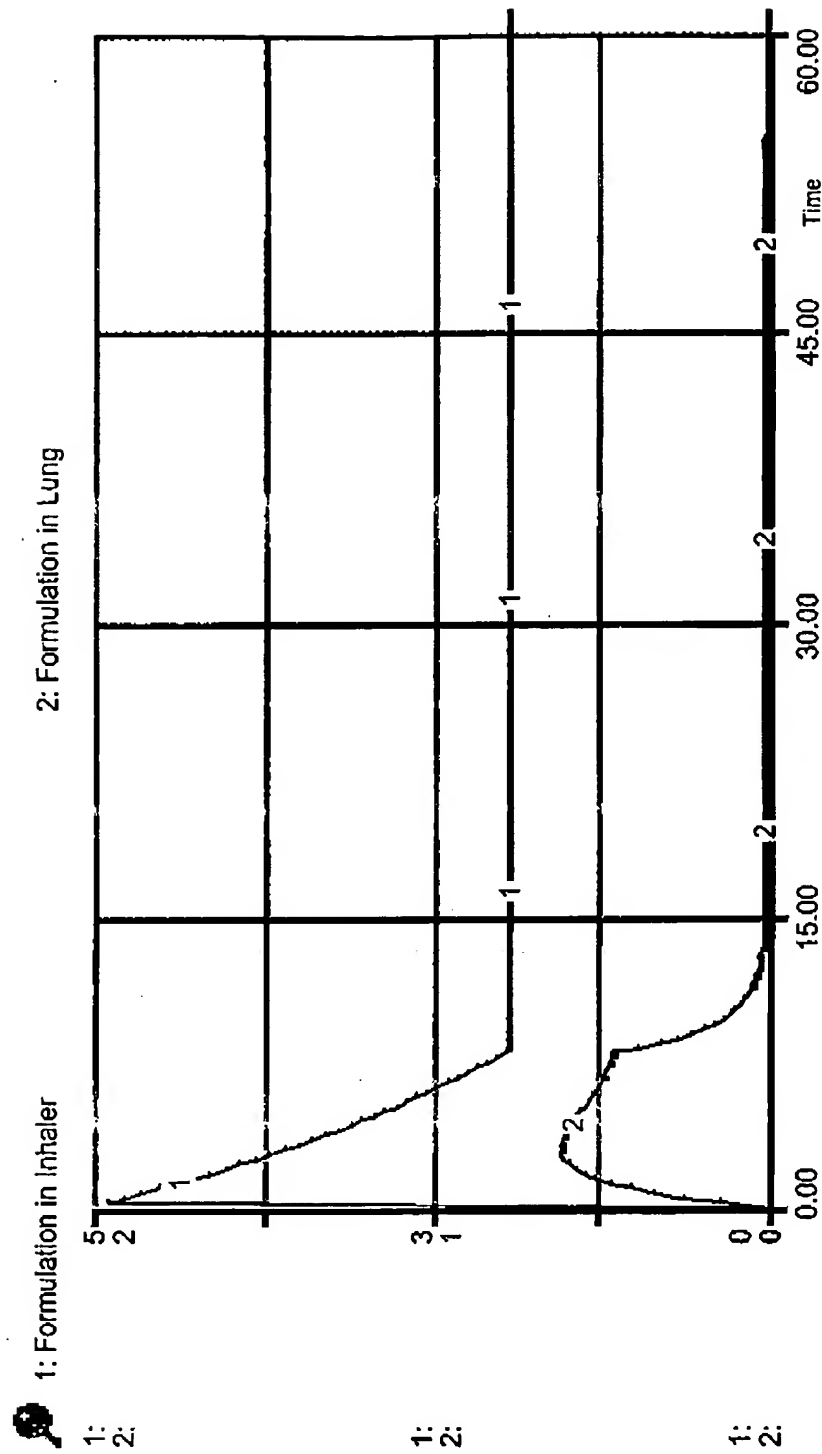
9/27

Figure 9



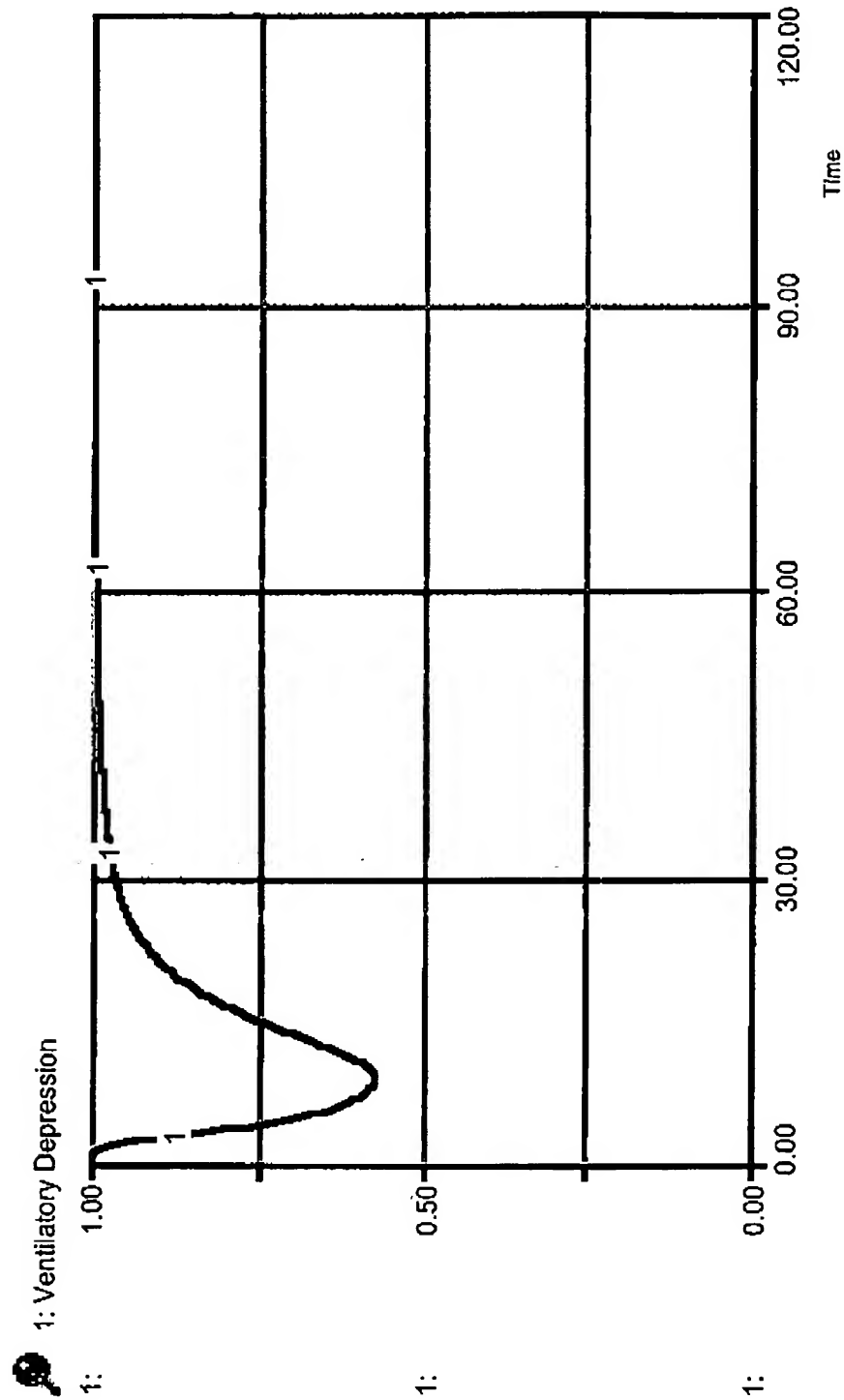
10/27

**Figure 10**



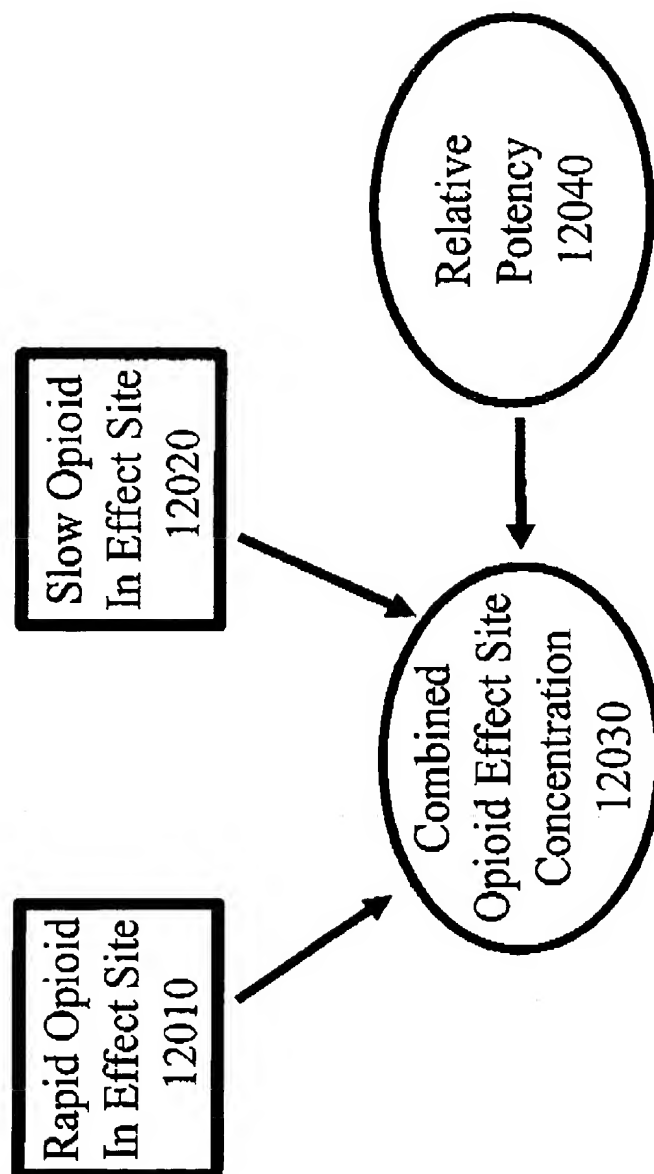
11/27

Figure 11

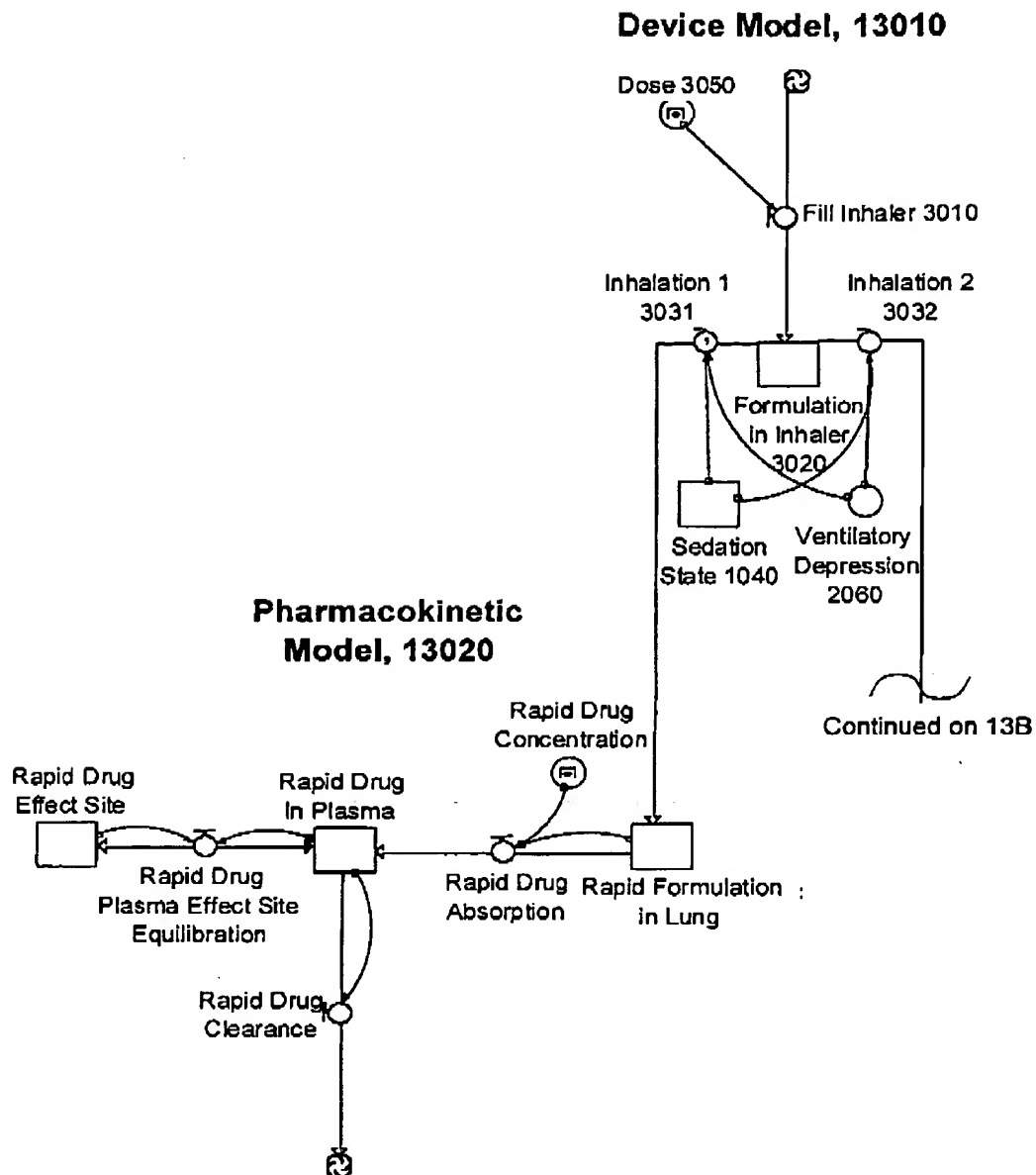


12/27

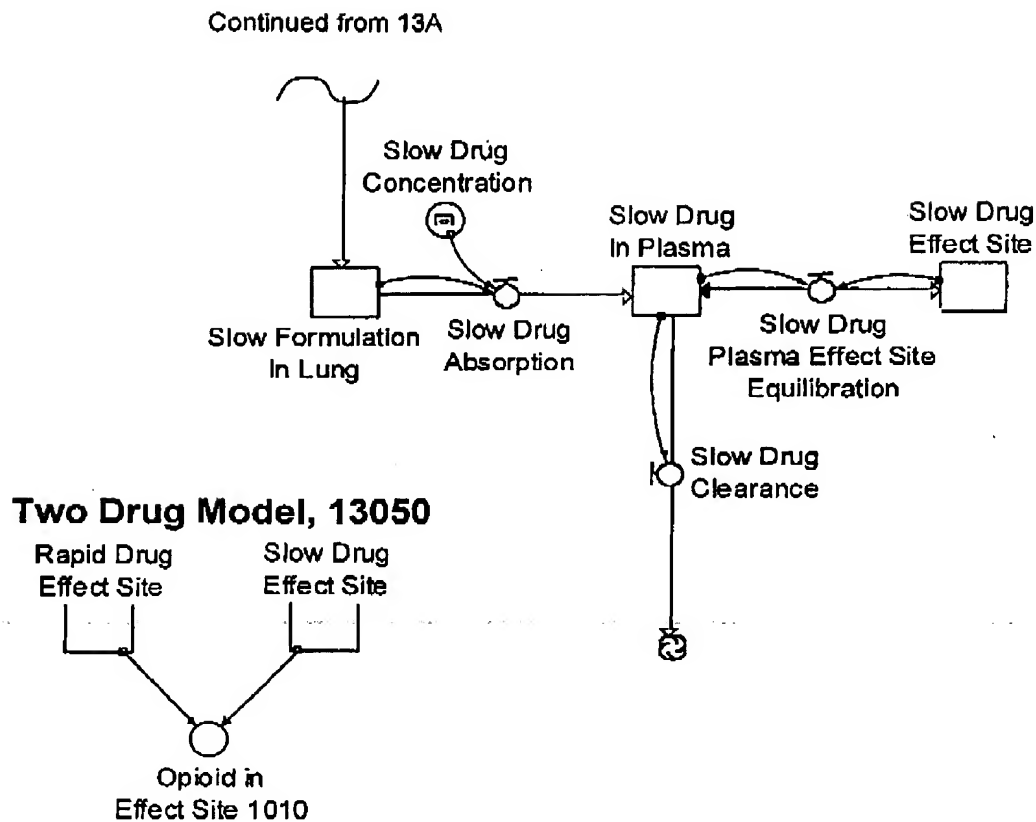
# Figure 12: Two Opioid Model



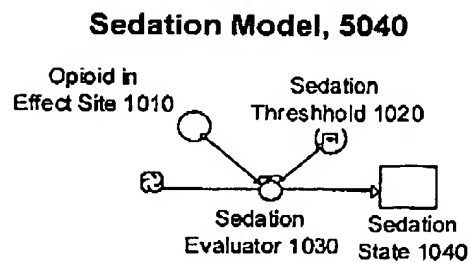
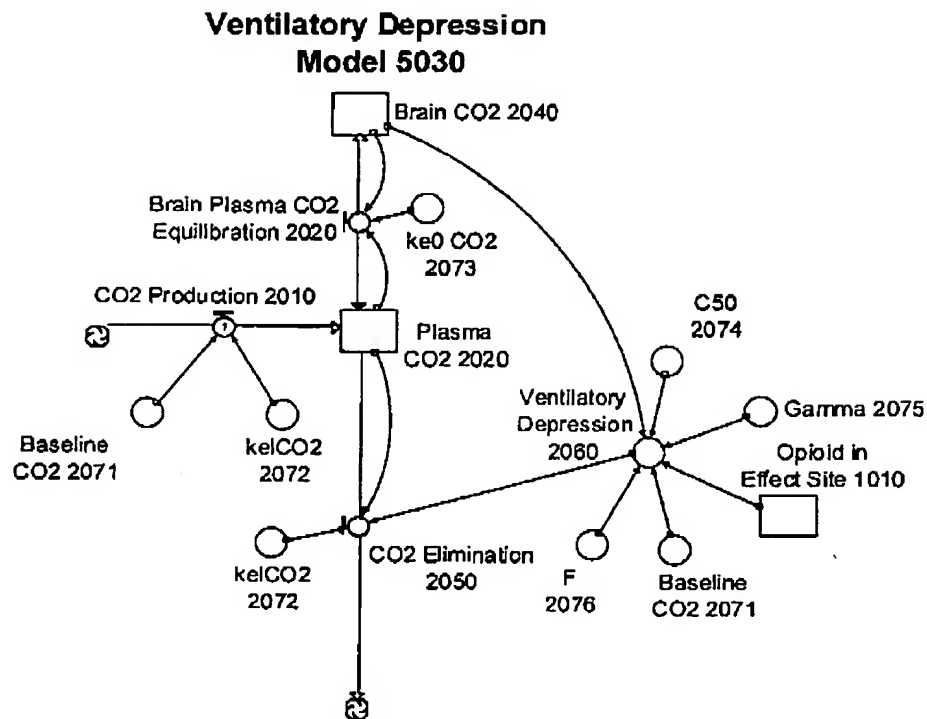
**Figure 13A:** The elements of the invention, wherein two opioids are administered through inhalation.



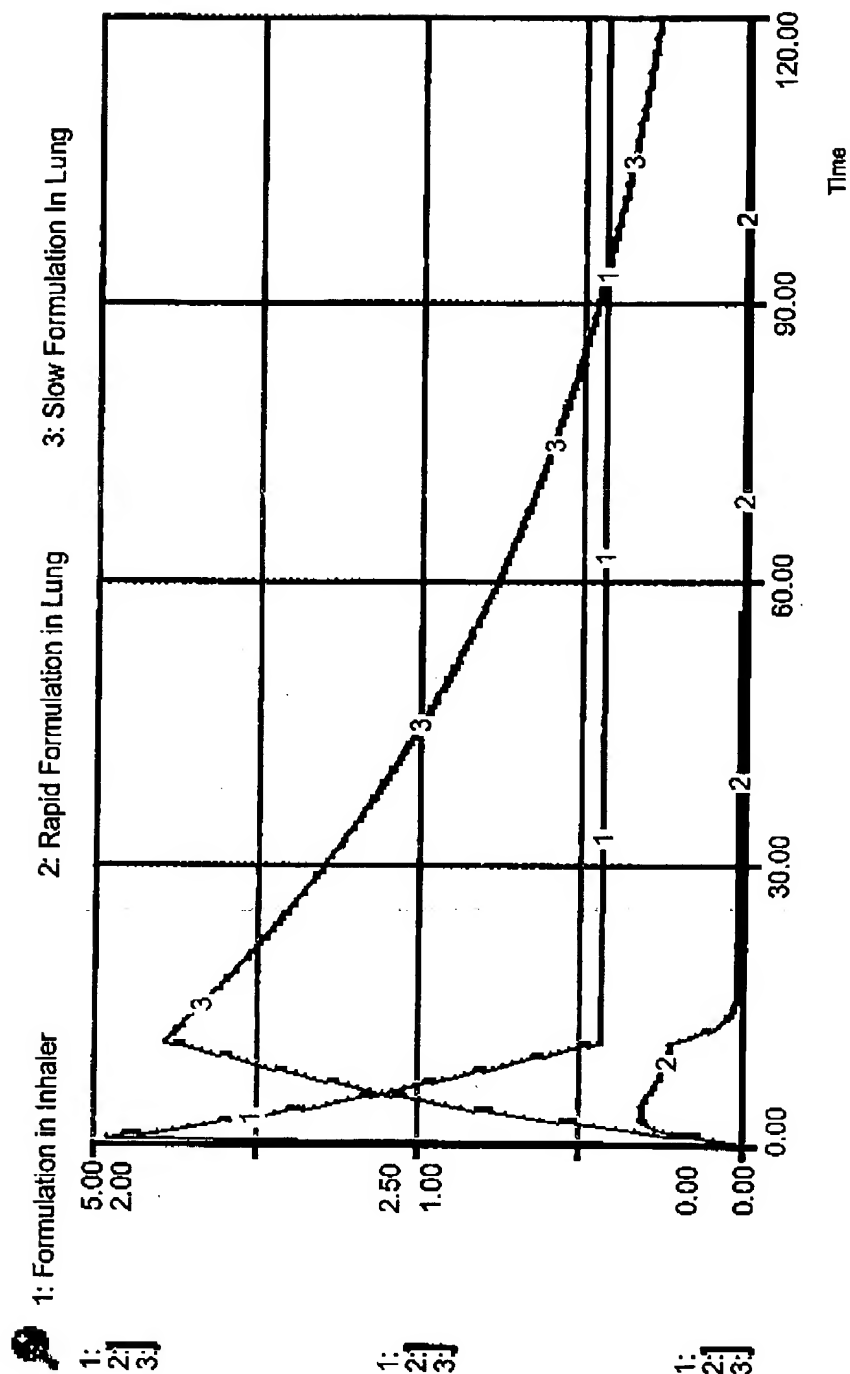
**Figure 13B** The elements of the invention, wherein two opioids are administered through inhalation.



**Figure 13C** The elements of the invention, wherein two opioids are administered through inhalation.

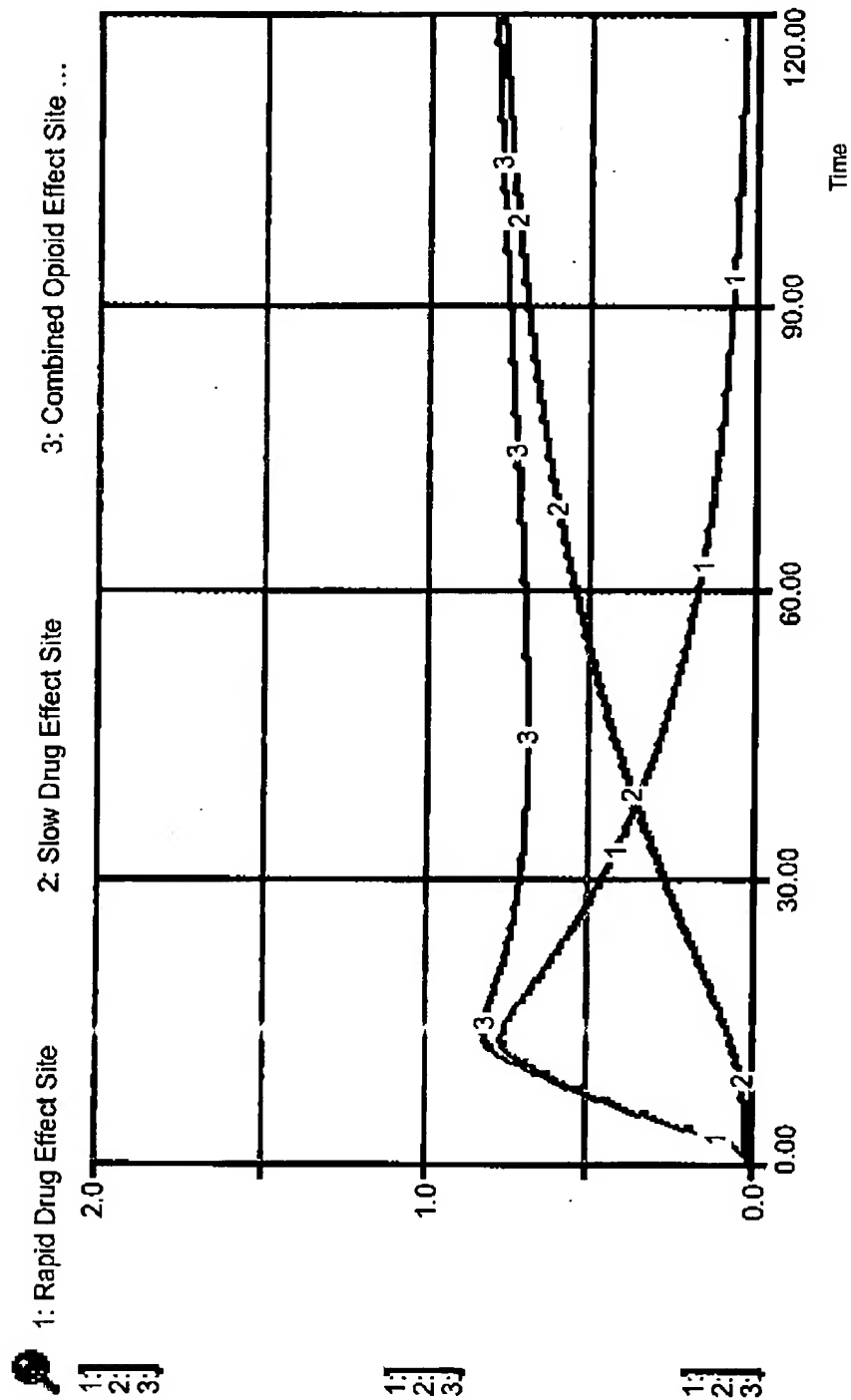


**Figure 14:** Drug in inhaler and lung in the presence of opioid-induced ventilatory depression and sedation for the two opioid model.

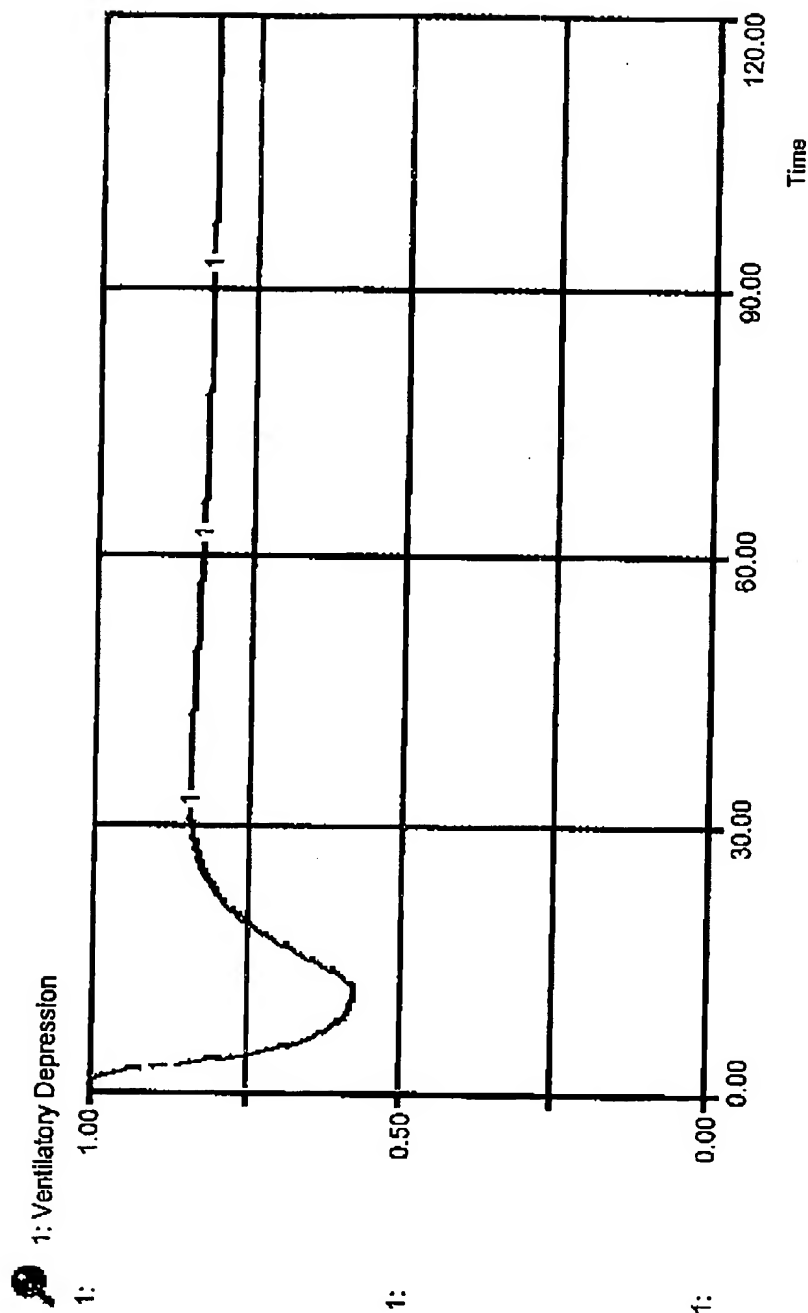


17/27

**Figure 15:** The rapidly acting opioid concentration in the effect site, the slowly acting opioid concentration in the effect site, and the combined concentration of opioid at the effect site, during two opioid administration with the device.

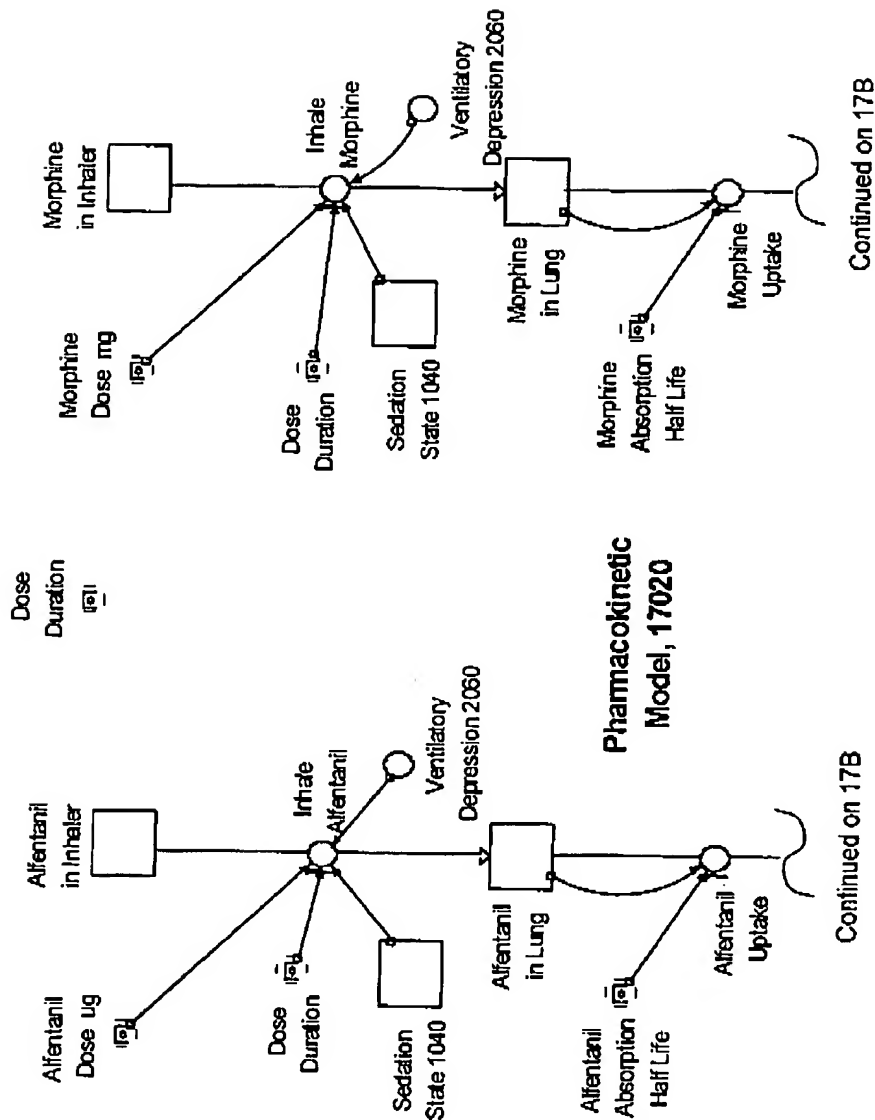


**Figure 16:** Ventilatory depression in the presence of self-limitation of opioid delivery from ventilatory depression and sedation with the two-opioid delivery system.

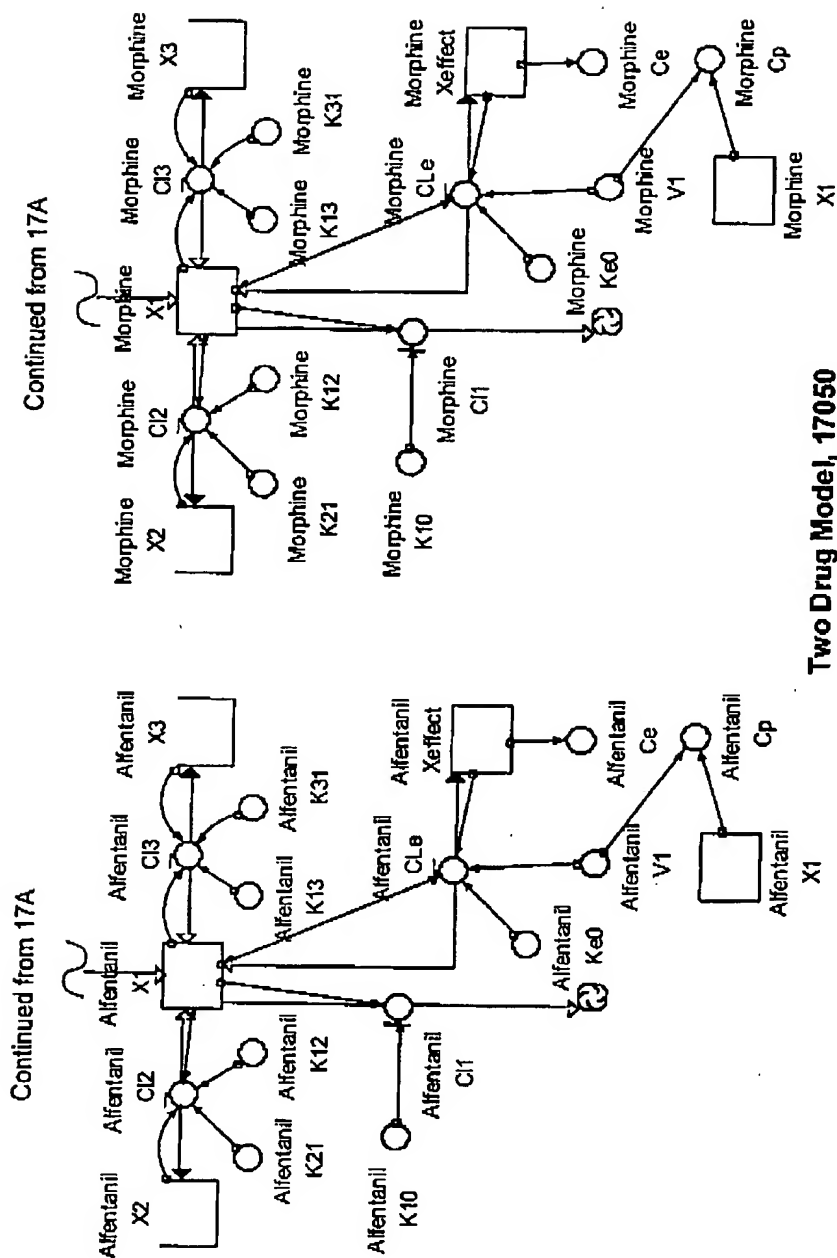


**Figure 17A:** The elements of the invention, wherein two opioids are administered through inhalation, and the rapidly acting opioid is alfentanil, and the slowly acting opioid is morphine.

### Device Model, 17010

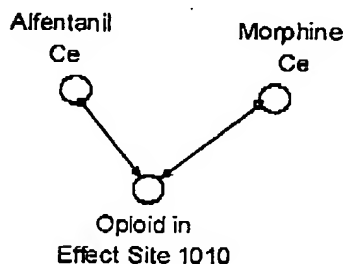


**Figure 17B:** The elements of the invention, wherein two opioids are administered through inhalation, and the rapidly acting opioid is alfentanil, and the slowly acting opioid is morphine.

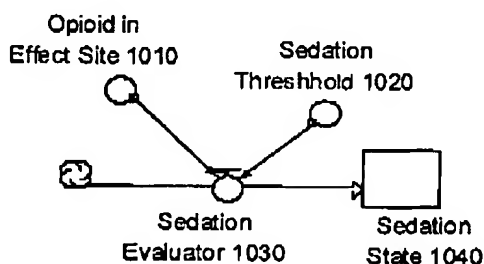


**Figure 17C:** The elements of the invention, wherein two opioids are administered through inhalation, and the rapidly acting opioid is alfentanil, and the slowly acting opioid is morphine.

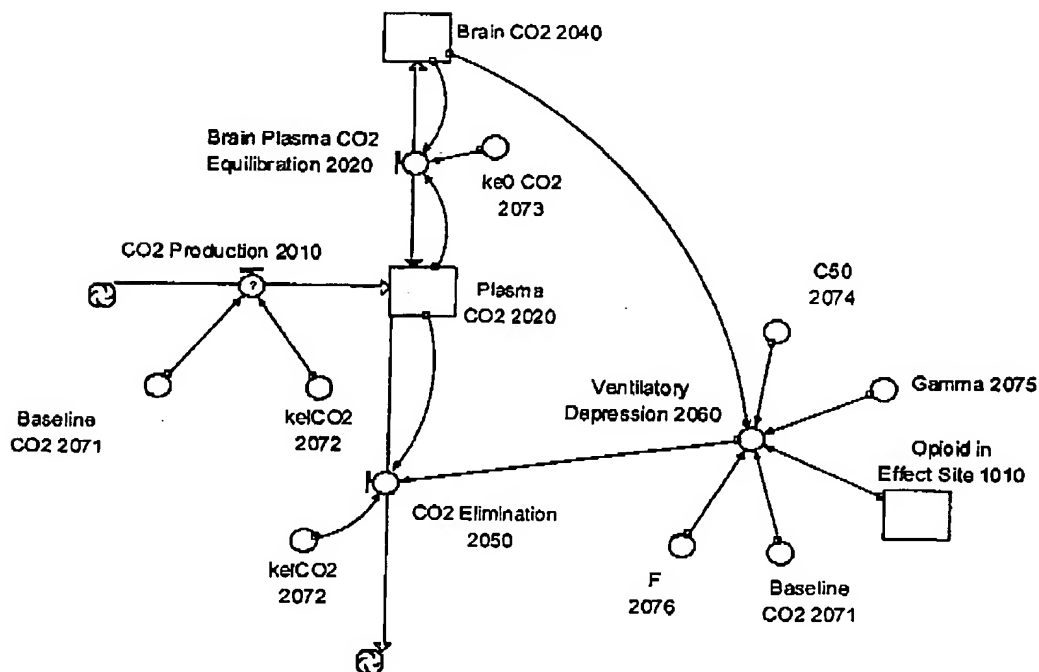
**Two Drug Model, 17050**



**Sedation Model 5040**



**Ventilatory Depression Model 5030**



22/27

Figure 18: Alfentanil, morphine, and combined opioid effect site concentrations.

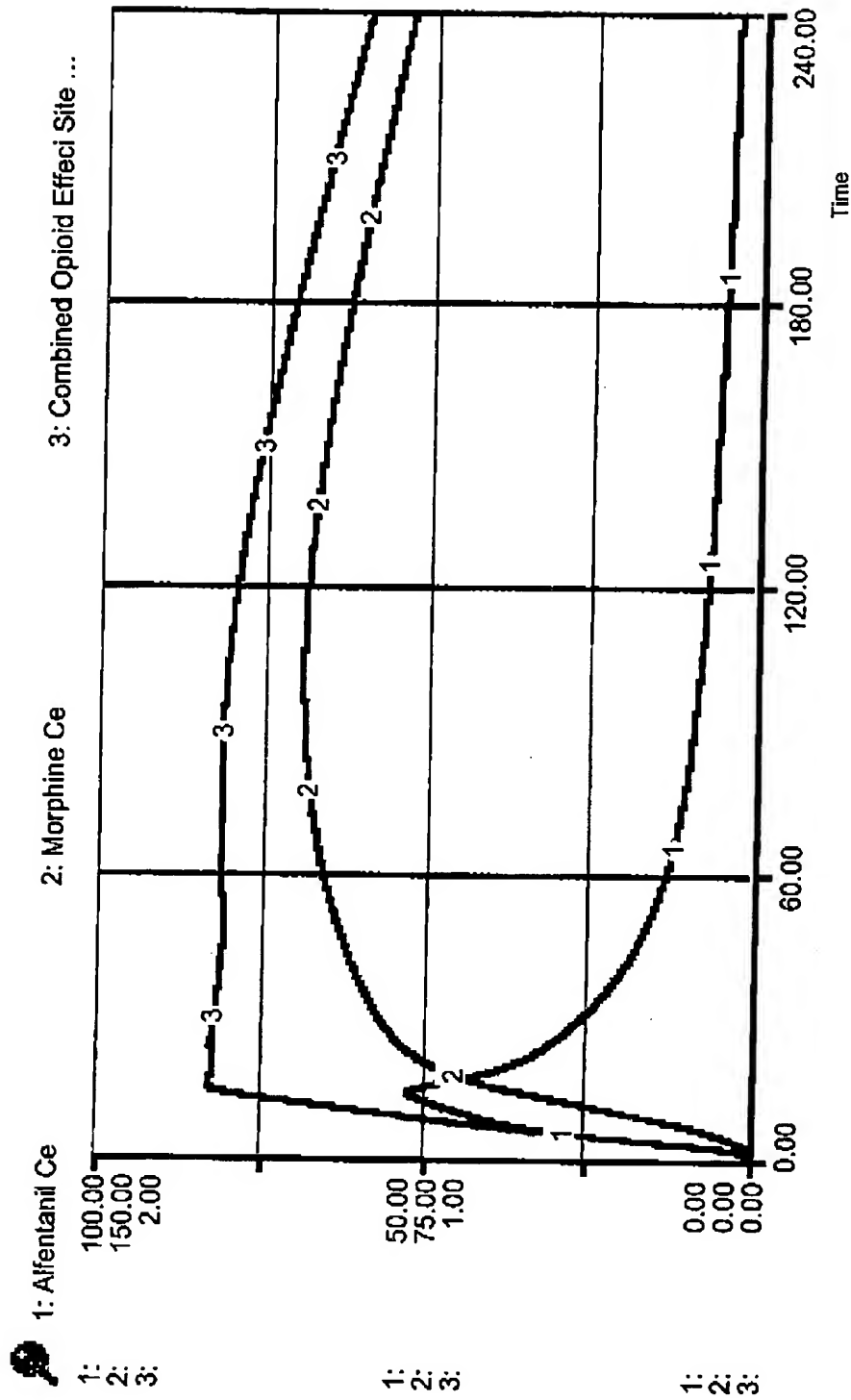
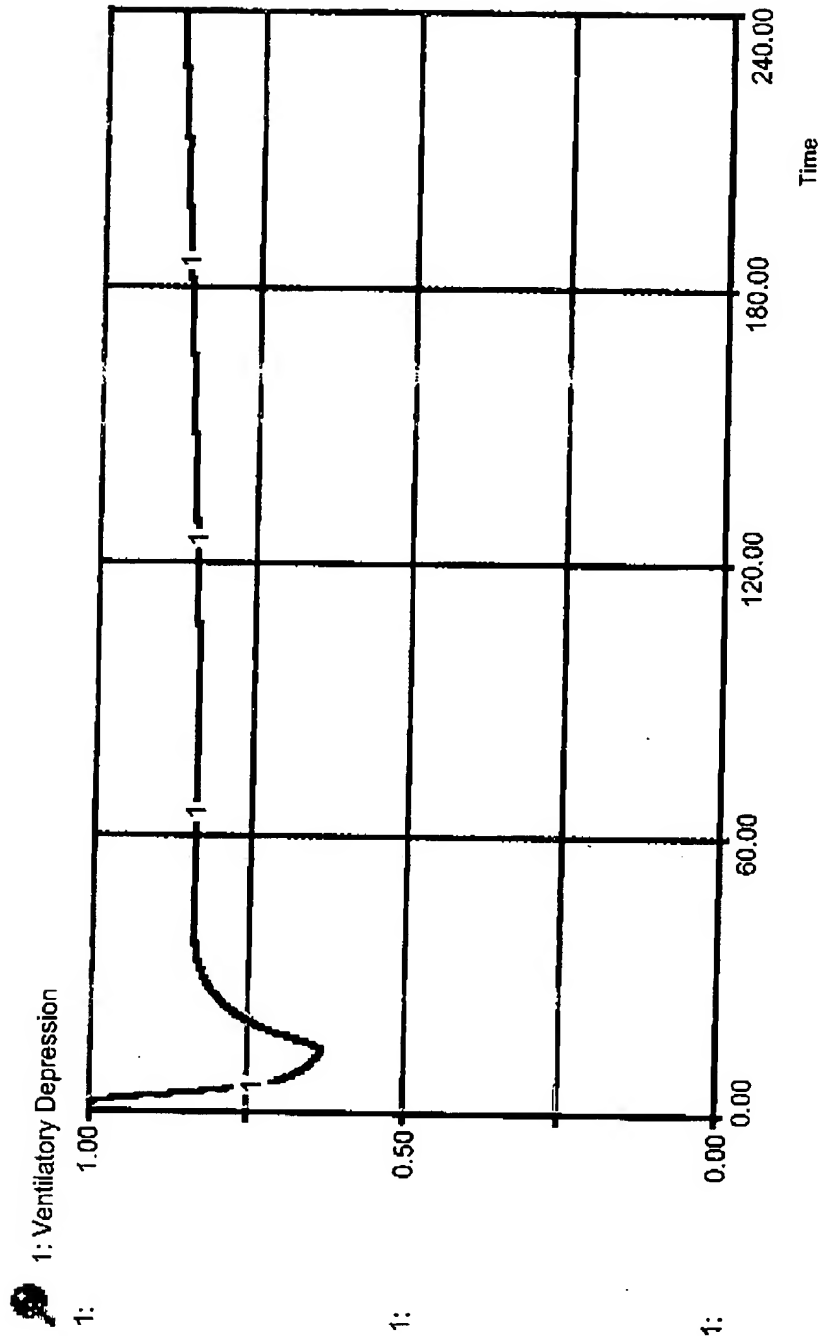
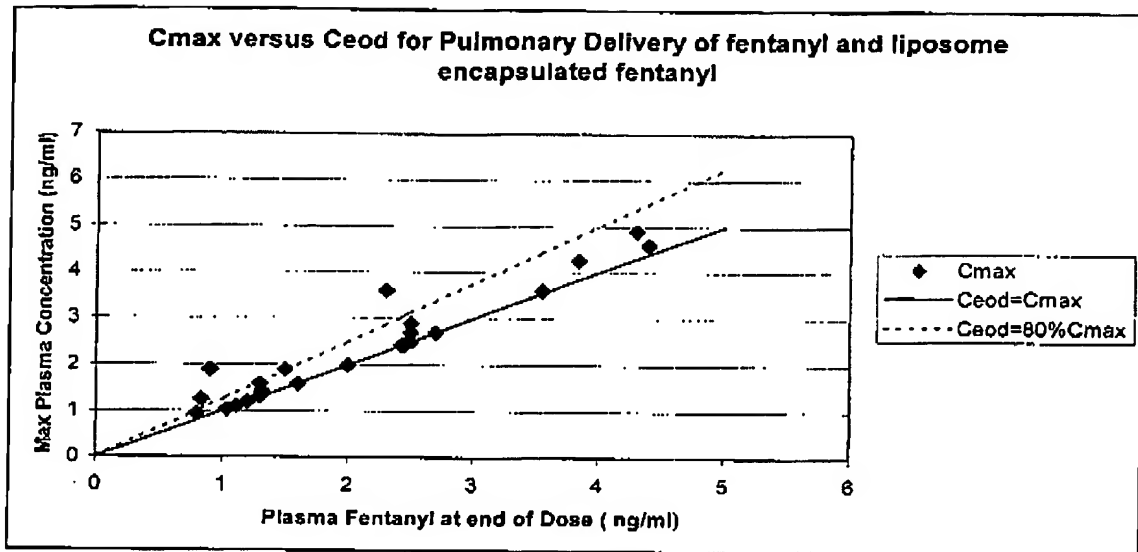
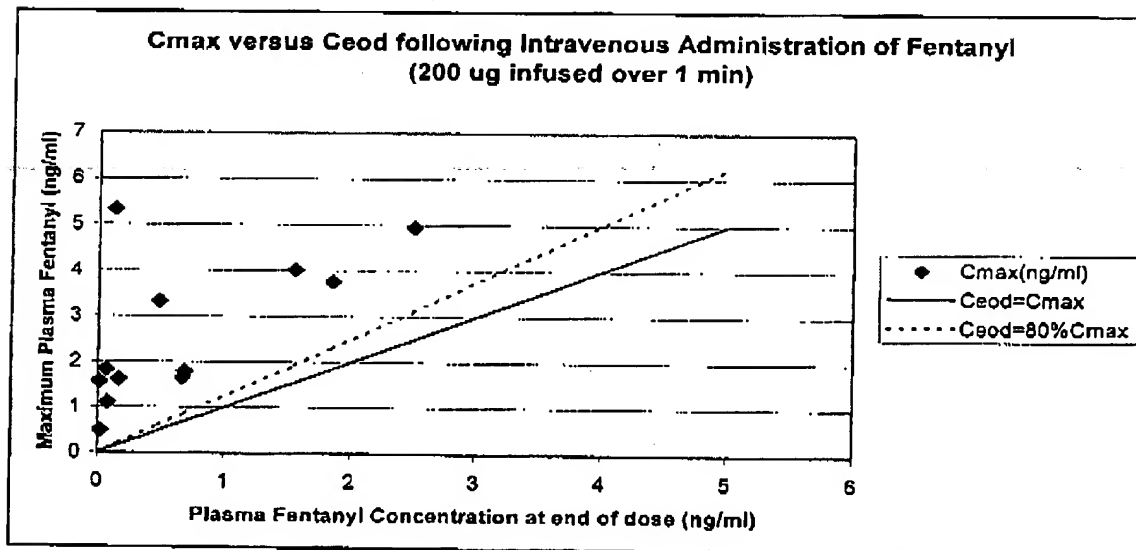
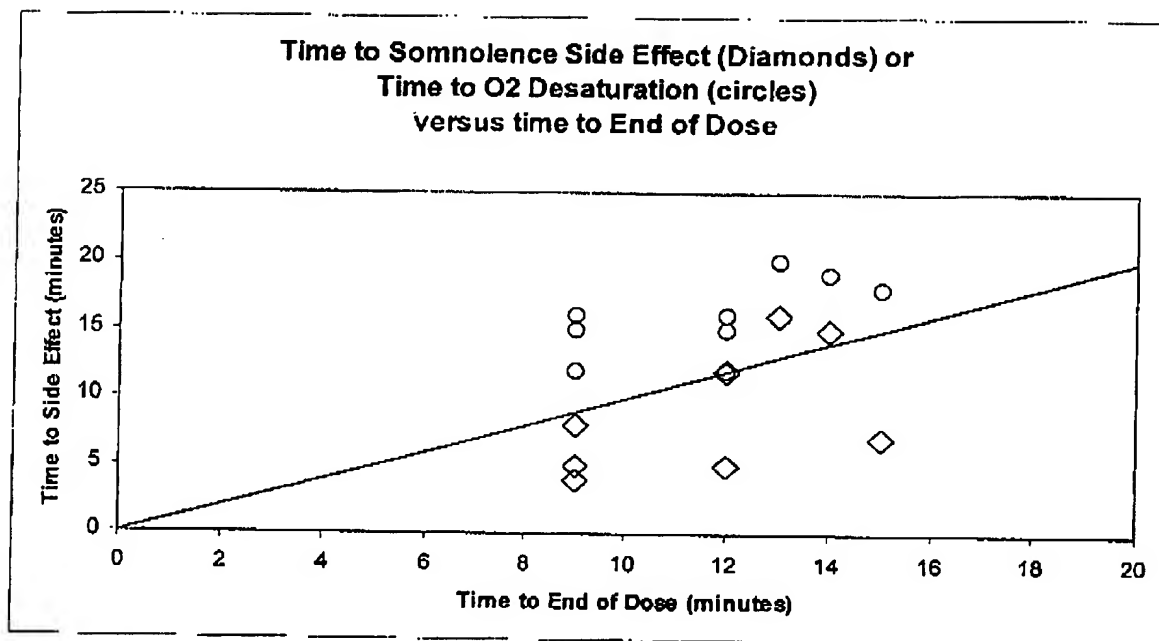


Figure 19



24/27

**Figure 20A****Figure 20B**

**Figure 21**

**Figure 22: Correlation of side effect to toxic event**

No side effect		Side effect	
N	26	24	
No hypoxia	22	14	36
Hypoxia	4	10	14
Null effect			
No hypoxia	18.72	17.28	36
Hypoxia	7.28	6.72	14
P value		0.038653124	